

1. A 1,4-substituted cyclic amine derivative represented by the following formula (I):

$$R^{1}$$
 $B-C$ R^{2}
 CH_{2} $T-(CH_{2})_{m}-Y$ $Z-R^{5}$
 R^{3} $(CH_{2})_{p}$

(I)

wherein A, B, C, D, and T are the same or different from one another and each represents methine or nitrogen, provided that one and only one of them represents nitrogen;

the bond represented by the following formula:

represents a single or double bond;

Y and Z are the same or different from each other and each represents methine, nitrogen, a group represented by the following formula:

or a group represented by the following formula:

provided at least one of them represents nitrogen;

 ${\sf R}^1$ and ${\sf R}^2$ are the same or different from each other and each represents

hydrogen, halogeno, hydroxy, lower alkylsulfonylaminoalkyl, lower halogenatedalkylsulfonylaminoalkyl, 2-pyrrolidinon-1-yl, 1-hydroxy-1-(methoxypyridyl)methyl, methoxypyridylcarbonyl, 1,3-propanesultum-2-yl, lower hydroxypiperidylcarbonylalkyl, lower hydroxyalkylamidoalkyl, lower halogenated-alkylamidoalkyl, lower dihalogenatedalkylamidoalkyl, lower heteroarylamidoalkyl, lower hydroxyalkylamidoalkyl, optionally substituted amino, nitro, lower alkyl, lower alkoxy, lower acyl, lower alkoxyalkoxy, cyano, lower alkylsulfonyl, sulfonylamido, hydroxy-lower alkyl, hydroxy-lower alkoxy, lower alkoxycarbonylamino, lower alkylsulfonylamino, N-lower alkylalkylsulfonylamino, lower acylamino, optionally substituted aminoalkyl, optionally N-substituted lower acylaminoalkyl, optionally substituted aryl, optionally substituted arylsulfonylamino, lower alkylsulfonyloxy, hydroxyiminomethyl, (2-pyrrolidon1-yl)methyl, (2-piperidon-1-yl)methyl, optionally substituted heteroaryl, optionally substituted aralkyl, optionally substituted heteroarylalkyl, cycloalkylcarbonylaminoalkyl, optionally substituted ureido, optionally substituted ureido-lower alkyl, succinimido, (succinimido-1-yl)lower alkyl, amido, optionally substituted carbamoyl, optionally substituted carbamoyl-lower alkyl, optionally substituted thiocarbamoyllower alkyl, formyl, aromatic acyl, heteroarylcarbonyl, halogenated lower alkyl, (2-imidazolidinon -1-yl)methyl, (2,4-imidazolidinedion-3-yl)methyl, (2-oxazolidon3-yl)methyl, (glutarimido-1-yl)methyl, optionally substituted heteroarylhydroxyalkyl, cyano-lower alkyl, 1-hydroxy lower cycloalkyl, (2,4-thiazolidinedion-3-yl)methyl, optionally substituted 4-piperidylmethyl, heteroarylacyl, pyrrolidinylcarbonyl-lower alkyl, optionally substituted aminosulfonylalkyl, carboxy-lower alkyl, or lower alkylamidoalkyl; or alternatively R¹ and R² together may form optionally substituted alicycle, optionally substituted heterocycle or alkylenedioxy, provided

these rings may be substituted;

R³ represents hydrogen, halogeno, lower alkyl, hydroxy, hydroxy-lower alkyl, lower alkoxy, formyl, optionally substituted aralkyloxy, hydroxy-lower alkoxy, optionally substituted sulfamoyl, or optionally N-substituted sulfamoyl-lower alkyl;

R⁴ represents hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkoxyalkyl, optionally aryl-substituted aryloxyalkyl, or optionally aryl-substituted aralkyloxyalkyl;

R⁵ represents lower alkyl, lower acyl, lower alkoxycarbonyl, aromatic acyl, or a group represented by the following formula:

$$-Q^{1}-(CH_{2})_{S}-Q^{2}-R^{6}$$

wherein Q^1 and Q^2 are both single bonds, or one of them is a single bond while the other represents oxygen, carbonyl, a group represented by -NHCO-, a group represented by -NHSO₂-, or a group represented by >CH-R⁷, wherein R⁷ represents hydroxy, lower alkyl or halogeno:

s represents 0 or an integer of 1 to 6; and

R⁶ represents optionally substituted aryl, optionally substituted heteroaryl, optionally substituted benzoheteroaryl, 1,4-benzodioxanyl, 1,3-benzodioxolyl, benzothiazolyl, or cyano;

n represents 1;

m represents 0 or an integer of 1 to 6; and

p represents an integer of 1 to 3,

and pharmacologically acceptable salts thereof.

A 1,4-substituted cyclic amine derivative represented by the following formula:

$$R - (CH_2)_m - Y Z - R^5$$

wherein R represents a substituent of the formula:

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wherein the bond represented by the following formula:

and R^1 , R^2 , R^3 , R^4 , R^5 , Y, Z, m, and p are each as defined in claim 1, and pharmacologically acceptable salts thereof.

- 3. The 1,4-substituted cyclic amine derivative as set forth in claim 1 or a pharmacologically acceptable salt thereof, wherein m is 0 and p is 2.
- 4. The 1,4-substituted cyclic amine derivative as set forth in claim 1 or a pharmacologically acceptable salt thereof, wherein Y is methine and Z is nitrogen.

5. The 1,4-substituted cyclic amine derivative as set forth in in claim 1 or a pharmacologically acceptable salt thereof, which is a compound selected from among the following ones:

(267)

- 1-{1-[2-(4-methoxyphenyl)ethyl]piperidin-4-yl}-7-methoxy-1,2,3,4-tetrahydroquinoline,
- (268) 1-{1-[2-(4-fluorophenyl)ethyl]piperidin-4-yl}-7-methoxy-1,2,3,4-tetrahydroquinoline,
- (269) 1-[1-(4-cyanopropyl)piperidin-4-yl]-7-methoxy-1,2,3,4-tetrahydroquinoline, (270)
- 1-{1-[2-(2-thienyl)ethyl]piperidin-4-yl}-7-methoxy-1,2,3,4-tetrahydroquinoline, (271)
- 1-{1-[2-(4-fluorophenyl)ethyl]piperidin-4-yl}-7,8-dimethoxy-1,2,3,4-tetrahydro-quinoline,
- (272) 1-{1-[2-(4-fluorophenyl)ethyl]piperidin-4-yl}-7,8-methylenedioxy-1,2,3,4-tetrahydroquinoline,
- (273) 1-{1-[2-(4-fluorophenyl)ethyl]piperidin-4-yl}-7-methoxy-8-methyl-1,2,3,4-tetrahydroquinoline,
- (274) 1-{1-[2-(4-fluorophenyl)-2-oxoethyl]piperidin-4-yl}-7-methoxy-1,2,3,4-tetrahydroquinoline,
- (275) 1-{1-[2-(4-fluorophenyl)-2-hydroxyethyl]piperidin-4-yl}-7-methoxy-1,2,3,4-tetrahydroquinoline,
- (276) 1-{1-[2-(4-fluorophenyl)-2-fluoroethyl]piperidin-4-yl}-7-methoxy-1,2,3,4-tetrahydroquinoline, and
- (283) 5-{4-[2-(4-fluorophenyl)ethyl]piperazin-1-yl}-5,6,7,8-tetrahydroisoquinoline.

- 6. A pharmaceutical composition comprising a therapeutically effective amount of the 1,4-substituted cyclic amine derivative or salt as set forth in claim 1 in combination with a pharmaceutically acceptable carrier.
- 7. An agent for treating, ameliorating, and preventing diseases against which serotonin antagonism is efficacious, which contain as the active ingredient the 1,4-substituted cyclic amine derivative as set forth in claim 1 or a pharmacologically acceptable salt thereof.
- 8. An agent for treating, ameliorating, and preventing spastic paralysis, which contain as the active ingredient the 1,4-substituted cyclic amine derivative as set forth in claim 1 or a pharmacologically acceptable salt thereof.
- 9. A muscle relaxant which contains as the active ingredient the 1,4-substituted cyclic amine derivative as set forth in claim 1 or a pharmacologically acceptable salt thereof.
- 10. A process for producing a 1,4-substituted cyclic amine derivative represented by the following formula:

$$R^1$$
 $B-C$ R^2 R^4 $N-R^5$ R^3 $(CH_2)_p$

wherein the bond represented by the following formula:

and A, B, C, D, R¹, R², R³, R⁴, R⁵, n, and p are each as defined in claim 1, which comprises removing, if necessary, the protecting group from a 1,4-substituted cyclic amine derivative (IX) represented by the following formula:

$$R^{1}$$
 B
 C
 R^{2}
 CH_{2}
 N
 R^{3}
 CH_{2}
 R^{4}
 N
 R^{5}
 CH_{2}
 R^{5}
 R^{4}
 R^{5}
 R

wherein the bond represented by the following formula:

and A, B, C, D, R^1 , R^2 , R^3 , R^4 , n, and p are each as defined in claim 1; and Pr.G represents hydrogen or a protecting group, and then reacting the same with L- R^5 wherein R^5 is as defined in claim 1; and L represents a leaving group.

11. A process for producing 1,4-substituted cyclic amine derivative (X), as set forth in claim 1, which comprises reacting a fused cyclic amine represented by the following formula:

wherein the bond represented by the following formula:

and A, B, C, D, R¹, R², R³ and n are each as defined in claim 1 with a cyclic ketone (VIII) represented by the following formula:

$$O = \begin{pmatrix} R^4 \\ N - Pr.G \\ (CH_2)_p \qquad (VIII) \end{pmatrix}$$

wherein R^4 , p, and Pr.G are each as defined in claim 1 in the presence of a reducing agent to thereby give a 1,4-substituted cyclic amine derivative (IX), removing, if necessary, the protecting group therefrom and further reacting the same with $L-R^5$.

12. A 4-substituted cyclic amine derivative represented by the following formula:

wherein the bond represented by the following formula:

and A, B, C, D, R^1 , R^2 , R^3 , R^4 , n, and p are each as defined in claim 1, provided that the case where R^1 , R^2 , R^3 and R^4 are all hydrogen atoms is excluded.

13. A method for treating a disease to which serotonin antagonism is efficacious, which comprises administering an effective dose of the 1,4-substituted cyclic amine derivative as set forth in claim 1, or a pharmacologically acceptable salt thereof, to a person in need of such treatment.

14. The 1,4-substituted cyclic amine derivative as set forth in claim 1, in which the bond represented by the following formula in the formula (I):

is a single bond, represented by the formula (XXI):

$$R^{1}$$
 B-C R^{2} D R^{4} (CH₂)_n-Y $Z-R^{5}$ (XXI)

or a pharmacologically acceptable salt thereof.

15. The 1,4-substituted cyclic amine derivative as set forth in claim 1, in which m is 0 in the formula (I), represented by the formula (XXII):

or a pharmacologically acceptable salt thereof.

16. The 1,4-substituted cyclic amine derivative as set forth in Claim 1, in which m is 1 to 6 in the formula (I) or a pharmacologically acceptable salt thereof.

17. A 1,4-substituted cyclic amine derivative represented by the formula (XXIII):

$$\begin{array}{c|c}
R & B-C & R^2 \\
X & X & D & R^4 \\
(CH_2)_n & T = Y & Z-R^5 \\
R^3 & (CH_2)_p & (XXIII)
\end{array}$$

or a pharmacologically acceptable salt thereof.

18. The 1,4-substituted cyclic amine derivative as set forth in claim 1, in which the bond represented by the following formula in the formula (I):

is a double bond, represented by the formula (XXIV):

or a pharmacologically acceptable salt thereof.

19. The 1,4-substituted cyclic amine derivative as set forth in claim 1, in which the T is nitrogen